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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/313,434	05/17/99	PODOLSKY	D 00786/432001

HM12/0703

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EXAMINER	
DUFFY,P	
ART UNIT	**PAPER NUMBER**
1645	15

DATE MAILED: 07/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)	
09/313,434	Podolsky	
Examiner	Group Art Unit	
Duffy	1645	

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 2-6-01 + 4-2-01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-12 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 1-12 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other_____

Office Action Summary

DETAILED ACTION

1. Applicants' responses of 2-26-01 and 3-38-01 have been entered into the record.

Priority

2. The status of nonprovisional parent application(s) (whether patented or abandoned) for which Applicant desires priority under 35 USC 120 should be updated. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Drawings

3. The drawings submitted with this application were declared informal by applicant. Accordingly they have not been reviewed by a draftsperson at this time. When formal drawings are submitted, the draftsperson will perform a review. Direct any inquires concerning drawing review to the Drawing Review Branch (703) 305-8404.

Specification

4. The title of the invention is not descriptive of the claimed invention. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

5. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing corneal epithelial wound healing comprising

contacting the cornea with intestinal trefoil factor (ITF) or enhancing fragment thereof in an amount sufficient to enhance corneal epithelial wound healing, it does not reasonably provide enablement for treatment of all eye disorders including keratitis (inflammation of the cornea of the eye) of any type or keratoconjunctivitis (the combined inflammation of the conjuctivia and cornea of the eye) of any type, ophthalmic herpes zoster, ocular inflammation, or scarring of the eye tissues (cicatricial penhigoid). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to any treatment of any eye disorder including keratitis (inflammation of the cornea of the eye) of any type or keratoconjunctivitis (the combined inflammation of the conjuctivia and cornea of the eye) of any type, ophthalmic herpes zoster, ocular inflammation, or scarring of the eye tissues (cicatricial penhigoid) using trefoil proteins. The specification teaches that the family of trefoil proteins will have at least one of the following properties (I) common structural domain, (ii) degree of amino acid nucleotides sequence homology or (iii) a common functional characteristic. The teachings of the specification at page 41-43 indicate that ITF is effective in enhancing corneal epithelial wound healing by enhancing of the migration of the epithelial cells across the wound. The ability of ITF is enhance migration of corneal epithelial cells is similar to two known growth factors that enhance corneal epithelial wound healing (TGFβ and TGFα) *in vivo*. However, the specification is devoid of any teaching of an effect of spasmolytic peptide (SP) or pS2 on corneal wound healing or any of ITF, SP or pS2 on keratitis (inflammation of the cornea of the eye) of any type or keratoconjunctivitis (the combined inflammation of the conjuctivia and cornea of the eye) of any type, ophthalmic herpes zoster, ocular inflammation, or scarring of the eye tissues (cicatricial penhigoid). The teachings

of the specification are not enabling for use of trefoil proteins in general or SP or pS2 in particular, in corneal wound healing because the art teaches that similar structure does not predict similar function. Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule (i.e. ITF). It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity or structural conformation results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Gerhold et al.[BioEssays, Volume 18, Number 12, pages 973-981{1996)]; Wells et al.[Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550 (1997)]; Russell et al.[Journal of Molecular Biology, Volume 244, pages 332-350 (1994)] and Attwood, [Science, 290:471-473, (29 October 2000)]. As a result, the use of SP or pS2 is not enabled for enhancing corneal epithelial wound healing. As to any of the other claimed disorders [including but not limited to keratitis (inflammation of the cornea of the eye) of any type or keratoconjunctivitis (the combined inflammation of the conjuctivia and cornea of the eye) of any type, ophthalmic herpes zoster,

ocular inflammation, or scarring of the eye tissues (cicatricial penhigoid)] the specification is not enabled for treatment of any of these eye disorders for the following reasons. Applicants specification fails to teach any effect of any disclosed trefoil protein on any inflammatory process such as scarring, mitogenesis, production of secondary inflammatory mediators. It is noted that Applicants own specification and the art teaches that growth factors that have been documented to enhance corneal would healing have disparate effects on inflammation. The specification teaches that TGFβ decrease mitogenesis, TGFα increases mitogenesis, whereas ITF and SP have no effect on mitogenesis. Thus, the similar functional property of enhancing corneal would healing by promotion of epithelial cell migration does not predict similar effects on mitogenesis. The art specifically teaches that epithelial growth factor promotes corneal wound healing but at the cost of an inflammatory reaction (Burling et al, American Journal of Veterinary Research 61(9):1150-1155, 2000). Thus, growth factors that promote wound healing may also promote inflammation. Neither the art, nor the specification as originally filed provides a clear cut correlation of the enhancement activity of corneal wound healing by growth factors with the ability of the same to treat any eye disorder or ocular inflammation. Therefore, in the absence of teachings in the specification that trefoil proteins mitigate ocular inflammation caused by conjunctivitis, herpes zoster or any other mechanism, the treatment of eye disorders or any inflammatory eye disorders is not enabled by this specification at the time of filing.

In the absence of further guidance from Applicants as to the would healing properties of similar trefoil proteins (SP or pS2) and the ability of such to mitigate or treat ocular inflammatory disorders or viral infections of the eye, and in view that the art teaches that the ability of a growth factor to enhance wound healing does not correlate with treatment or mitigation of ocular inflammation or viral infections of the eye, it would require undue experimentation on the part of

the skilled artisan to so broadly use trefoil proteins for treatment of any aspect of any eye disorder including inflammation as claimed. As such, the claims should be so limited.

6. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the phrase "treatment of an eye disorder" however the claims never recite what aspect of the disorder(s) are positively affected or mitigated. As such, the metes and bounds of "treatment" can not be ascertained.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 2, 6, 7, 8, and 12 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wilson, U.S. Patent No. 5,703,047 issued December 30 1997.

Wilson teaches the promotion of corneal epithelial wound healing with growth factors (HGF and KGF) including human derived growth factors (EGF and TGFα) using topically applied factors (see column 4, lines 9-29; column 7 first full paragraph; column 12, second full paragraph and paragraph bridging columns 12-13) in relevant models. Since the specification describes the family of trefoil proteins as having at least one of the following properties (I) common structural domain, (ii) degree of amino acid sequence homology or (iii) a common functional characteristic (see page 7, third full paragraph), the growth factors of Wilson employed in the treatment of eye

disorders including corneal epithelial wound healing and dry eye are anticipated because the growth factors of the prior art have a common functional characteristic.

Status of Claims

9. No claims are allowed.

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
June 29, 2001

PDuffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600